A PRELIMINARY COMPARATIVE STUDY ON THE EFFICACY OF QUINAPYRAMINE SULPHATE/CHLORIDE AND MELARSOPROL IN RATS, EXPERIMENTALLY INFECTED WITH *TRYPANOSOMA EVANSI*

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**Summary**


Using standard parasitological, pathological, haematological and sero-biochemical methods, the trypanocidal effect of quinapyramine sulphate/chloride and melarsoprol has been compared in rats experimentally infected with *Trypanosoma evansi* isolated from a camel. The results indicated that infection in all rats resulted in fulminating parasitaemia (> 10⁶ trypanosomes per mL). One week after treatment, no parasitaemia was detected at necropsy in quinapyramine-treated rats but it was evident at a range of (5×10⁵ to 5×10⁶) in the positive control rats and in the melarsoprol-treated rats. Treatment with both drugs did not significantly influence the infection-induced changes in the PCV. The activities of ASAT and AP were significantly increased in groups II, III and IV. Treatment with melarsoprol insignificantly increased the concentration of urea in serum. There were no consistent differences in the overall histopathological pictures of the vital organs of infected and untreated rats as well as those treated with either drug following infection. It was concluded that, at the doses used, quinapyramine was effective in treating the strain of *T. evansi* used in this work while melarsoprol was not.

**Key words**: melarsoprol, quinapyramine sulphate/chloride, rats, *Trypanosoma evansi*

**INTRODUCTION**

*Trypanosoma evansi* is a common parasite in the tropics that causes a serious and economically important disease in domestic animals. The disease is known to occur in Northern Africa, Sudan, Eritrea, Ethiopia, Somalia, the Middle and Near East, the Indian subcontinent, Central Asia and the Far East (Mahmoud and Gray, 1980). Natural infections occur in camels, horses, bovine and dogs (Al-Rawashdeh *et al.*, 1999). In Saudi Arabia natural infections occur mainly in camels and the disease is vernacularly known as "Heyam". Results obtained from a field survey carried out by Omer *et al.* (1998) showed that 19.7% of sampled camels were serologically positive for trypanosomiasis by the passive haemagglutination test and 13.8% by Ag-ELISA.
The acute form of the disease is characterized by progressive anaemia, high fever, anorexia, loss of condition and often rapid death. The chronic form which is more common shows relapsing parasitaemia with or without pyrexia, emaciation, oedema of the abdomen and legs, abortion and death in some animals (Haroun et al., 2000). The main pathological features include degenerative and necrotic changes involving various organs (Raisinghani et al., 1980; Haroun et al., 2000).

For several decades now, not more than three drugs have been available for the treatment of camels afflicted with trypanosomiasis, and cases of resistance of different trypanosomes to nearly all the available drugs have been reported (Zhang et al., 1993; Scott et al., 1997). Lack of interest by the pharmaceutical industry to venture into development of new antitrypanosomal drugs has been a major stimulus for intensification of research into the few existing drugs (reviewed by Kinabo, 1993).

The present investigation was designed to compare the efficacy of an established drug, quinapyramine sulphate/chloride with the newest antitrypanosomal drug melarsoprol in rats experimentally infected with Trypanosoma evansi, a common parasite in the Central Region of Saudi Arabia.

MATERIALS AND METHODS

Twenty-four male Wistar rats (160 ± 10 g) were housed in a room at a temperature of 22 ± 2 °C and relative humidity of 50-60%, with artificial light from 5.00 a.m. to 4.00 p.m. Animals had free access to tap water and standard rat chow.

The rats were randomly divided into four equal groups, designated group I, II, III and IV.

Animals in groups II, III and IV were injected intraperitoneally with 1 × 10^5 trypanosomes isolated from a camel that was naturally infected with T. evansi. The rats in group I were kept as uninfected untreated controls, and those in group II served as infected untreated controls. Three weeks post infection, rats in group III were injected subcutaneously with a single dose of quinapyramine sulphate and quinapyramine chloride salts, in the ratio of 3:2 (Triquin®, Wockhart Ltd., Mumbai, India), at 8.3 mg/kg (0.05 mL/kg, from a suspension of 166.7 mg/mL water). Rats in group IV were injected intramuscularly with a single dose melarsoprol (Cymelarsan®, Rhône Mérieux, France), at 0.5 mg/kg. The animals in groups III and IV were killed one week after treatment.

Wet blood smears and Giemsa-stained thin blood films were prepared daily from the tail veins of all infected rats to assess infectivity. Parasitaemia was estimated by examining 200 microscopic fields. Three rats in group II were sacrificed in extremis on days 23 and 24 post infection. The rest of the animals were anaesthetized with diethyl ether and decapitated 4 weeks post infection. Blood was collected from all rats in plain and EDTA-containing tubes. The serum obtained was stored at –20 °C until used (within 5–10 days).

Necropsies were performed on all rats and specimens from lungs, liver, heart, kidneys and spleen were fixed in 10% neutral buffered formalin and were embedded in paraffin wax, sectioned at 5 µm and stained with haematoxylin and eosin (H/E) for examination by light microscopy.

Serum samples were analyzed for the activities of aspartate aminotransferase (ASAT) and alkaline phosphatase (AP) and for concentrations of total protein.
albumin, globulin and urea using commercial kits (Bio-Mérieux Reagents and Products, France). The packed cell volume (PCV) was measured using a microhaematocrit centrifuge (Hawkesly and Sons, Ltd. UK). Statistical comparisons were made using a one-way ANOVA followed by Neuman-Keuls multiple comparison test.

RESULTS

Three weeks post infection, all infected rats had a fulminating parasitaemia (> 10⁶ trypanosomes per mL). No parasitaemia was detected at necropsy in rats in group III (quinapyramine-treated), but it was evident at the range of (5×10⁵ to 5×10⁶) in rats of group II (positive controls) and group IV (melarsoprol - treated).

Splenomegaly was the main post mortem finding in rats in groups II, III and IV (Fig. 1). The weights of those spleens were approximately three times those of the rats in group I (negative controls). In the former 3 groups, slight congestion was observed in the heart, liver and kidneys. There were no consistent differences in the overall histopathological pictures of the vital organs of infected and untreated rats and those which had been infected and treated with either drug. The histopathological changes mainly comprised liver necrosis of some hepatic cells indicated by pyknosis, karyorrhexis and karyolysis. Disruption of hepatic cords due to necrosis and replacement by inflammatory cells was evident. The inflammatory cells were mainly mononuclear cells infiltrating the portal triads and surrounding the blood vessels leading to perivascular cuffing. In the kidneys, there were haemorrhagic, degenerative and necrotic changes in the tubular epithelium. Glomerulonephritis indicated by proliferation of mononuclear cells was observed. The white pulp of the spleen was hyperplastic and expanding and showed some fatty changes. The heart showed areas of infarction and haemorrhages. Many bronchial walls were thick-

![Fig. 1. Splenomegaly in a Trypanosoma evansi experimentally-infected rat.](image)
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and diminazene aceturate) that are effective in cattle, sheep, goats and equines may not be suitable for camels because of ineffectiveness and/or toxicity (Homeida et al., 1981; Ali and Hassan, 1986). Therefore there is a clear need for new, safe and effective drugs against T. evansi.

Quinapyramine salts have long been in use in the treatment T. evansi in camels and experimentally-infected laboratory animals. They are considered the “standard” drugs against which other drugs are evaluated (e.g. Ali et al., 1986). A decade or so ago, melarsoprol was marketed as a new effective therapeutic agent against T. evansi (Nyang’ao et al., 1995).

In the present limited trial, quinapyramine was found to be effective in apparently removing all T. evansi in rat’s blood. However, parasitaemia persisted one week after treatment with melarsoprol. The pathological and biochemical alterations induced by the experimental infection were, on the whole, not positively affected by treatment with either drug. This may be related to the short duration allowed after treatment (one week). However, quinapyramine seemed to have caused slightly more beneficial effects than Melarsoprol®. Thus the results of the present experiment seem to confirm the established efficacy of Triquin® against T. evansi. Melarsoprol however was found to be ineffective against the infection in rats at a dose of 0.5 mg/kg bodyweight. The ineffectiveness of this drug at the recommended dose of 0.25 mg/kg has previously been reported in buffaloes treated at doses ranging from 0.25 mg/kg to 3 mg/kg (Lun et al., 1991), in goats treated at a dose of 0.3 mg/kg (Zweygarth et al., 1992), in mice treated at doses of 0.25 mg and 0.5 mg/kg (Syakalima et al., 1995) and in cattle treated at a dose of 0.5 mg/kg (Payne et al., 1994). Musa et al. (1994) on the other hand found melarsoprol to be effective against T. evansi in camels at a dose rate of 0.25 or 0.5 mg/kg bodyweight. This probably confirms the suggestion made by Zweygarth et al. (1992) that the recommended dose might have been applied strictly for the treatment of camels only and that higher doses are needed to treat T. evansi in other animals. The same may be extended to rats used in the present work. It is possible that these rats were under-treated. Also the strain of T. evansi used could have been resistant to the effect of the drug.

Further experiments using a wider range of doses of quinapyramine and melarsoprol are warranted.

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